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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,549	04/01/2002	Michio Kubota	KUBOTA=9	3265

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EXAMINER	
RAO, MANJUNATH N	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 02/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,549	KUBOTA ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *16-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 April 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-42 are currently pending and are present for examination. Claims 1-15 are now under consideration. Claims 16-42 remain withdrawn from consideration as being drawn to non-elected invention.

Election/Restrictions

Applicants election of Group I, claims 1-15 with traverse in the paper submitted on 11-10-03 is acknowledged. Examiner also acknowledges the species election (SEQ ID NO:11) with traverse. The traversal is on the ground(s) that a unity of invention exists and that the restriction is improper and that, **claim**, not a partial reading of the claims, share the same or corresponding technical features and that no prior art has been cited. Examiner respectfully disagrees that unity exists for the reasons reiterated below. The lack of unity is not based on partial reading of claims. To reiterate, pursuant to 37 C.F.R. 1.475 (d), the ISA/US considers that where multiple products and processes are claimed, the main invention shall consist of the first invention of the category first mentioned in the claims and the first recited invention of each of the other categories related thereto. Accordingly, the main invention (Group I) comprises the first-recited product, an α-isomaltosylglucosaccharide-forming enzyme, a method for producing said enzyme and a method of using said enzyme. Further pursuant to 37 C.F.R. 1.475 (d), the ISA/US considers that any feature which the subsequently recited products and methods share with the main invention does not constitute a special technical feature within the meaning of PCT Rule 13.2 and that each of such products and methods accordingly defines a separate invention.

Applicants also argue that it would not constitute undue burden on the Examiner to examine both groups. Examiner respectfully disagrees with such an argument. The search for Group I alone involves extensive search of the patent databases, sequence databases and also non-patent literature databases. Therefore, examining group II would cause a serious burden to the Examiner.

Regarding election of species, applicants argue that all species share the same special technical feature and that there is no serious burden to search at least some of the species. Examiner respectfully disagrees with applicant's argument. Applicants have included 9 different amino acid sequences. With the addition of several thousand sequences every day into the public databases as well as the PTO's sequence database, searching all the sequences included by the applicant would cause a serious burden on the Examiner. Examiner also disagrees with the applicants that they will be required to file additional eight applications, because election of species will not involve filing separate applications for each species.

For all the above reasons, the requirement is still deemed proper and is therefore made FINAL.

Claims 16-42 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper filed on 11-10-03.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). ***Drawings***

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Information Disclosure Statement

There is no submission of a list of references in the specification in a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered. The references have been placed in the application file, but the information referred to therein has not been considered.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6, 8-15 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1-15 are drawn to "an α-isomaltosylglucosaccharide-forming enzyme" and method of making it and using it which as written reads on the product of nature. Amending the claim to recite "an isolated or purified α-isomaltosylglucosaccharide-forming enzyme....." to show the hand of man would overcome this rejection. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 and claims 2-15 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-2 recite the phrase "substantially increasing the reducing power". The metes and bounds of the above phrase are not clear to the Examiner. A perusal of the specification did not provide the Examiner with a specific definition for the above phrase rendering the claims indefinite.

Claim 2 and claims 3-15 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 2 recites the phrase "substantially incapable of..". The metes and bounds of the above phrase are not clear to the Examiner. A perusal of the specification did not provide the Examiner with a specific definition for the above phrase rendering the claims indefinite.

Claim 4 and claims 5-15 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 recites the phrase "substantially increasing the reducing power". The metes and bounds of the above phrase are not clear to the

Examiner. A perusal of the specification did not provide the Examiner with a specific definition for the above phrase rendering the claims indefinite.

Claim 4 and claims 5-15 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 (part 6) recites the phrase "50 ° C or lower" and so on. The metes and bounds of the above phrase specifically the of word "lower" are not clear to the Examiner. A perusal of the specification did not provide the Examiner with a specific definition for the above phrase rendering the claims indefinite.

Claim 4 and claims 5-15 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 recites the phrase "having a stable pH region". It is not clear to the Examiner as to what applicants mean by the above phrase. It appears that applicants intended to recite "having activity in the pH region" to claim that the enzyme was active in the pH range of 4.5 to 10 thereby indicating that the enzyme was stable at those pH values. However, the claim as written does not refer to activity at all rendering the claim unclear. Correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-11 are rejected because the invention appears to employ novel microorganisms. Since the microorganisms are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The microorganisms required for the isolation of the enzyme are not fully disclosed, nor have all the methods required to obtain them been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the microorganisms. The specification does not disclose a repeatable process to obtain the microorganisms and it is not apparent if the microorganisms are readily available to the public. Accordingly, it is deemed that a deposit of these plasmids should have been made in accordance with 37 CFR 1.801-1.809.

It is noted that applicants have deposited the organisms but there is no indication in the specification as to public availability. If the deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;

2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and

4. the deposit will be replaced if it should ever become inviable.

Claims 1-4, 6-8, 12-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isomaltosylglucosaccharide-forming enzyme (IMG) isolated from *Bacillus* sp., or *Arthrobacter sp.*, wherein said enzyme comprises SEQ ID NO:11, and wherein said enzyme forms a saccharide having a glucose polymerization degree of at least three with both, an α-1,6-glucosidic linkage (as a linkage at the non-reducing end) and the α 1,4-glucosidic linkage (other than the linkage at the non-reducing end) by catalyzing the α glucosyl transfer from a saccharide having glucose polymerization of at least two and having α 1,4-glucosidic linkage as a linkage at the non-reducing end does not reasonably provide enablement for any such enzyme isolated from any or all sources including recombinant mutants and variants and having a broad molecular weight ranging from 74,000 to about 160,000 Daltons, or a broad isoelectric point range of about 3.8 to about 7.8 or having thermostability at 45 ° C or lower (wherein the lower value can be any temperature value) when incubated at pH 6.0 for 60 min, or having a broad pH stability between pH 4.5 to about 10.0 at 4 ° C for 24 hours. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-4, 6-8, 12-15 are so broad as to encompass any IMG from any source including recombinant mutants and variants and having a broad molecular weight ranging from 74,000 to about 160,000 Daltons, or a broad isoelectric point range of about 3.8 to about 7.8 or having thermostability at 45 ° C or lower (wherein the lower value can be any temperature value) when incubated at pH 6.0 for 60 min, or having a broad pH stability between pH 4.5 to about 10.0 at 4 ° C for 24 hours. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of IMG's broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a single IMG isolated from *Bacillus* species or *Arthrobacter sp.*, wherein said enzyme comprises SEQ ID

NO:11, and wherein said enzyme forms a saccharide having a glucose polymerization degree of at least three with both, an α-1,6-glucosidic linkage (as a linkage at the non-reducing end) and the α 1,4-glucosidic linkage (other than the linkage at the non-reducing end) by catalyzing the α glucosyl transfer from a saccharide having glucose polymerization of at least two and having α 1,4-glucosidic linkage as a linkage at the non-reducing end. It would require undue experimentation of the skilled artisan to make and use the polypeptides as claimed by the applicants. The specification is limited to teaching the use of a polypeptide comprising SEQ ID NO: 11 as an IMG but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any or all IMG from any source including recombinants, mutants and variants and having a broad molecular weight ranging from 74,000 to about 160,000 Daltons, or a broad isoelectric point range of about 3.8 to about 7.8 or having thermostability at 45 ° C or lower (wherein the lower value can be any temperature value) when incubated at pH 6.0 for 60 min, or having a broad pH stability between pH 4.5 to about 10.0 at 4 ° C for 24 hours etc. because the specification does not establish: (A) a rational and predictable scheme for isolation of any IMG from any source having a broad molecular weight ranging from 74,000 to about 160,000 Daltons, or a broad isoelectric point range of about 3.8 to about 7.8 or having thermostability at 45 ° C or lower (wherein the lower value can be any temperature value) when incubated at pH 6.0 for 60 min, or having a broad pH stability between pH 4.5 to about 10.0 at 4 ° C for 24 hours etc; (B)regions of the protein structure which may be modified without affecting IMG activity; (C) the general tolerance of IMG polypeptides to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any amino acid residue in a polypeptide comprising SEQ ID NO:11 with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including IMGs from all or any sources or with an enormous number of amino acid modifications to the polypeptide comprising SEQ ID NO:11. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ

19 24 (CCPA 1970)). Without sufficient guidance, determination of IMGs having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1-3, 6-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-3, 6-15 are directed to polypeptides having IMG activity. Claims 1-3, 6-15 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides including modified polypeptide sequences, that have not been disclosed in the specification. No description has been provided of the polypeptide sequences encompassed by the claim. No information, beyond the characterization of the IMG polypeptide as comprising SEQ ID NO:11 has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides. The specification does not contain any disclosure of the structure of the polypeptide sequences, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of structures. Therefore many structurally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species (IMG comprising amino acid sequence SEQ ID NO:11) of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot

reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 5 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 5 is directed to a genus of IMG comprising a specific 9 amino acid long peptide sequence. As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The specification fails to describe any other representative species by sufficient identifying characteristics (i.e., considerable amino acid sequence

information) or properties to show that applicant was in possession of the claimed genus. The identifying characteristics recited in claim 5, --limited to enzymatic activity (depending from claim 1), and the 9 amino acid sequence (SEQ ID NO:11) which constitutes a minor aspect of the structural description-- does not include sufficient characteristics to limit the claimed genus to proteins which are not highly variable in both structure and function. The claims include species in which a large percent of the amino acid sequence (depending on the total number of amino acids in the polypeptide) of the single disclosed species has been substituted as well as allowing alterations in functional characteristics such as substrate specificity, temperature optima, pH optima, and inhibitor/activator profiles. Therefore, the species within the genus are highly variable in both structure and function. While claim 5 add a single additional characteristic to the limitations of the genus (i.e., comprising SEQ ID NO:11) this characteristic, by itself is not sufficient to change the fact that the claims include proteins which are highly variable in both structure and function. Thus for all the reasons discussed, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

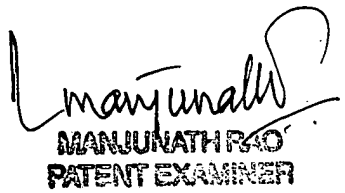
Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The examiner can normally be reached on 6.30 a.m. to 3.00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0939. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.



Manjunath N. Rao
January 28, 2004